BY ORDER OF THE SECRETARY OF THE AIR FORCE

AIR FORCE INSTRUCTION 40-402

19 JULY 1994

Medical Command

USING HUMAN SUBJECTS IN RESEARCH, DEVELOPMENT, TEST, AND EVALUATION

COMPLIANCE WITH THIS PUBLICATION IS MANDATORY

OPR: HQ AFMOA (Col Gerald J. Merritt)
Certified by: HQ AFMOA (Col Jacqueline Morgan)
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This instruction implements AFPD 40-4, *Clinical Investigation and Human Use in Medical Research.* It provides guidance and procedures for using human subjects in research, development, test, and evaluation (RDT&E) conducted or funded by the Air Force. For programs using animals in RDT&E, refer to AFI 40-401, *The Use of Animals in DoD Programs* (formerly AFR 169-2). Refer to AFI 40-403, *Clinical Investigations in Medical Research, Guidance and Procedures* (formerly AFR 169-6), when using humans as subjects of clinical investigations. Under exceptional circumstances, you may request an exception to one or more of the procedures in this instruction. Submit all requests for a waiver through command channels to HQ AFMOA/SGPT. Give a full justification for the waiver. Only the US Air Force Surgeon General can grant a waiver. This instruction directs collecting and maintaining information subject to the *Privacy Act of 1974* authorized by 10 U.S.C. 55 and 10 U.S.C. 8013. System of Records F168 AF SG C applies. Send comments and suggested improvements on AF Form 847, **Recommendation for Change of Publication**, through channels, to HQ AFMOA/SGPT, 170 Luke Avenue, Suite 400, Bolling AFB DC 203332-5113.

SUMMARY OF REVISIONS

This the initial publication of AFI 40-402, substantially revises AFR 169-3, *Use of Human*

Subjects in Research, Development, Test and Evaluation, 15 July 1985; incorporates reference to the *Policy for the Protection of Human Subjects* (32 CFR 219); requires the investigator to comply with 32 CFR 219, the local human-use committee to monitor compliance, and all facilities engaged in research to provide written assurance of compliance; and does not repeat any instructions or definition of terms which are included in 32 CFR 219.

Section A—Research Covered by This Instruction

1. Description. This instruction applies to the following research, whether it is conducted by the Air Force, a contractor, grantee, or other agency using Air Force funds:

- Biomedical research and behavioral studies involving human subjects.
- RDT&E involving new drugs, vaccines, biologicals, or investigational medical devices.
- Research that includes human subjects, whether as the direct object of research or as the indirect object of research, where such research involves more than minimal human risk in the development and testing of military weapon systems, vehicles, aircraft, and other materiel.
- Research activities funded by non-Air Force resources in which the human subjects are Air Force military or civilian personnel.

1.1. Research, as defined in this instruction, does not include individual or group training of military personnel such as combat readiness, effectiveness, proficiency, or fitness exercises. It also does not include epidemiological surveys that are of no more than minimal risk.

Section B—Air Force Responsibilities

2. The Surgeon General:

- Establishes an Air Force Human Use Committee (HUC) under HQ Air Force Medical Operations Agency (AFMOA).
- Renders final decision on all protocols involving investigational use of drugs, devices, and radiopharmaceuticals.

3. The Air Force HUC:

- Approves or disapproves all protocols that do not involve investigational use of drugs, devices, and radiopharmaceuticals.
- Reviews and recommends protocols involving investigational drugs, devices, and radiopharmaceuticals to the Air Force Surgeon General for final approval.
- Notifies the major command (MAJCOM) and the organization submitting the protocol of approval or disapproval.
- Reviews all reports of misadventure or unanticipated medical events involving a human subject in a research protocol.
- Reviews all requests for waiver from this instruction.
- Reviews and approves statements from organization commanders that give assurance of compliance with the federal policy for the protection of human subjects in research under 32 CFR 219.103, *Assuring Compliance with Policy on Protection of Human Subjects*. Issues either a single-project or multiple-project assurance number.

4. MAJCOM. The Air Force Materiel Command (AFMC) establishes and operates RDT&E laboratories to support the aerospace mission.

5. The Organization Commander:

5.1. Ensures compliance with 32 CFR 219, *Protection of Human Subjects*, and appoints a local HUC.

5.2. Before involving human subjects in research, sends HQ AFMOA/SGPT 170 Luke Avenue, Suite 400, Bolling AFB DC 20332-5113 written assurance of compliance with policies on *Protection of Human Subjects* as detailed in 32 CFR 219.103.

5.3. Refers any controversial protocols on which the local HUC needs additional guidance in the use of human subjects to HQ AFMOA/SGPT through medical staff channels.

5.4. Approves or disapproves protocols after review by the local HUC. If the local HUC recommends safeguards or special conditions for a protocol, the commander must not reduce these safeguards or conditions in approving the protocol. The commander may require additional safeguards, may disapprove the protocol, or may refer the protocol to a higher review and approving authority. The commander may not approve a project that the local HUC recommends for disapproval.

5.5. Submits all protocols or tests in which human subjects would be exposed to more than minimal risk to the Air Force HUC for approval before beginning the protocol or test and provides an information copy of the protocol to the MAJCOM surgeon. Submits all documentation, including the protocol, minutes of the local HUC review, consent documents, Food and Drug Administration (FDA) approval, if applicable, and commander's recommendation for approval for review.

5.6. Reports any medical misadventures or unanticipated medical events to HQ AFMOA/SGPT, (RCS: HAF-SG(AR)8501, *Medical Misadventure Report*) within 5 wokdays.

- Transmits initial reports electronically as quickly as possible to HQ AFMOA/SGPT if the misadventure or unanticipate medical event is lifethreatening or otherwise serious.

6. The Local HUC:

6.1. Monitors compliance with 32 CFR 219.

6.2. Reviews all human-use protocols, assures their scientific merit, and determines the acceptability of using human subjects.

6.3. Determines whether a particular investigation involves more than minimal risk.

6.4. Reviews all informed consent documents to ensure compliance with 32 CFR 219.116.

6.5. Applies the following criteria when reviewing and approving protocols:

- The protocol contributes significantly to an approved Air Force research program, and has reasonable prospects of yielding important results, essential to such programs, which are not obtainable by other methods or means of study.
- Human subjects used in a protocol are kept to the minimum number which will reasonably achieve the required scientifically valid results.
- The protocol is to be conducted to avoid all unnecessary physical or mental discomfort, suffering, or injury.
- Sufficient animal or laboratory experiments or other evaluations have been completed if there is any inherent reason to believe that death or disabling injury is remotely possible, to give assurance of acceptable risk before use of human subjects.
- The degree of risk to be taken never exceeds that required by the urgency or importance of the Air Force research program to which the study is related.
- Proper preparations are made, and adequate facilities provided, to protect the human subject against all reasonable, foreseeable possibilities of injury, disability, or death.

- The protocol is to be conducted only by persons possessing the requisite scientific qualifications. The highest degree of skill and care will be required during all stages of the study from persons who conduct or assist in the study.
- Human subjects have no physical conditions which will make participation more hazardous for them than it would be for normal healthy persons, unless such condition is a necessary prerequisite for the specific protocol involved. The use of human subjects with such preexisting conditions must be specifically approved by the Air Force HUC.
- The scientifically or technically qualified person conducting the protocol and each member of the research team, is prepared to terminate the subject's participation at any stage if there is any reason to believe, in the exercise of good faith, superior skill, and careful judgment, that continuation is likely to result in injury, disability, or death to the human subject.
- There is no greater intrusion into the privacy of the human subject than is absolutely necessary for the conduct of the protocol involved.

6.6. Ensures compliance with FDA regulations in the application and approval procedure for use of investigational drugs and devices.

6.7. Sends recommendation for approval or disapproval of protocols to the organization commander.

6.8. Maintains records of:

- Assurance numbers issued by DHHS and HQ AFMOA/SGPT.
- Human-use protocols reviewed or approved.
- Informed consent documents for all subjects.
- Progress and final reports submitted by investigators.
- Reports of injuries to subjects.
- Minutes of HUC meetings prepared in compliance with 32 CFR 219.115.
- Continuing review activities as required by 32 CFR 219.109.
- All protocol-related correspondence.
- HUC members identified by name, office, earned degrees, and representative capacity.

7. The Principal Investigator:

7.1. Complies with AFPD 40-4 and 32 CFR 219 in the use of human subjects during the course of the investigation.

7.2. Ensures the overall safety of the human subjects used in the study.

7.3. Prepares the research protocol and informed consent document and submits them to the the local HUC. Attaches sample consent documents and other appropriate study documentation to the protocol. (See sample format in **Attachment 2**).

7.3.1. At a minimum, the protocol must contain:

- The objectives of the project.
- The method and means for achieving the objectives.
- An analysis of potential risk to human subjects and contraindications.

- Safety measures.
- Other means for reducing risks to human subjects.
- The names of the principal and associate investigators and the designated medical monitor.

7.3.2. Investigators may use a generic protocol when the research project involves the use of human subjects in a group of closely related and similar studies that differ from each other in ways that are not likely to change the degree of risk. The variations within the research project must be minor deviations in the interventional procedures that do not alter the risk to the subject.

- A generic protocol does not contain a detailed plan of every possible test that might be undertaken; it includes the boundary conditions for all potential risks and procedures that might apply in the future in this area and the standards for safeguarding subjects. A generic protocol must discuss in detail the necessary equipment, including safety equipment, that will be used, with all conditions to which the subjects will be exposed and the tolerable deviation from normal vital signs outside of which subjects will be suspended from further participation.
- Using generic protocols is acceptable only if the proposed study conditions are so well understood that the described safety limits are clearly acceptable to the subject. Sample consent documents are part of the generic protocol submission.
- The Air Force HUC must approve all generic protocols. Such approval will last for a specific time period (generally 2 years), subject to renewal. However, since a generic protocol does not permit evaluation of all factors before approval of a particular test, the organization's HUC and commander must approve each generic protocol test before it may be accomplished.

7.4. Submits the appropriate forms to the FDA if the protocol involves the use of a new drug or device according to 21 CFR 300-499. Attaches to the protocol copies of FDA approvals for the use of drugs and devices.

7.5. Conducts and supervises the study and records data in appropriate documents relating to the research protocol. Records medical tests or laboratory procedures, procedures performed, drugs administered, and significant observations (including effects) in each subject's medical record.

7.6. Sends all proposed changes to the protocol or informed consent document to the local HUC and Air Force HUC for approval, if required, before protocol implementation.

7.7. Submits one copy of the following reports to HQ AFMOA/SGPT through the local HUC and commander, with an information copy to the MAJCOM surgeon:

- Annual progress reports, including a copy of any study-related abstract, oral presentation, technical report, or journal article. Must submit a separate report on each human-use study. See AFI 40-403, attachment 6, for a sample progress report format.
- Final report of the findings and conclusions of the investigation, either when completed or when terminated for other reasons. If indicated, make suggestions for the application of findings and possible additional research.
- Medical Misadventures or Unanticipated Medical Events Report within 24 hours of an event's occurrence. Submit reports to the organization HUC and commander on any misadventure or unanticipated medical event that coincides with, or possibly results from, using human sub-

jects in research protocols (RCS: HAF-SG (AR8501), *Medical Misadventure Report*). Submit more detailed narrative reports to the organization HUC and commander within 15 workdays of the misadventure or unanticipate medical event. The initial report within 24 hours of the event should contain:

- Brief description of the extent and severity of the injuries and the identity of the person injured (including name, age, sex, military or civilian status, and social security number).
- Explanation of how the injuries occurred.
- Time, date, and place of incident.
- Name, address, and telephone number of the organization official authorized to provide additional information.
- This report is designated emergency status Code C-3. Continue reporting during emergency conditions, delayed precedence. Submit data requirements as prescribed, but they may be delayed to allow the submission of higher precedence reports. Submit by nonelectronic means if possible. Discontinue reporting during MINIMIZE.

Section C—Use of Human Subjects in RDT&E

8. When To Use Human Subjects. Investigators use human subjects only in mission-related or mission-essential research protocols when investigators cannot get the desired data from valid animal studies, computer-modeling techniques, or other reliable nonhuman techniques.

8.1. Note that investigators must use nonhuman subjects and nonliving analogs (such as dummies or phantoms) when human subjects are not required by the nature of the research. Investigators must always use nonhuman subjects for studies in which irreversible injury is expected to occur.

8.2. Allow the following categories of personnel to participate as subjects:

- Military personnel may participate as human subjects. However, give consideration to how their participation in the protocol may affect their ability to mobilize for readiness, to perform duties, or to be available for duty. The Air Force prohibits additional compensation for such services except as specifically authorized by law.
- Retired military personnel, dependents, and others routinely entitled to medical care in military medical facilities may participate as human subjects. Such persons may receive compensation for these services as authorized by applicable directives (45 Comptroller General 649), except that retired officers of a regular component are subject to the limitations of 5 U.S.C. 5532.
- Private citizens. US Policy is not to accept voluntary services (without compensation) when such services may provide a basis for a future claim against the Government for the value of the services provided or for personal injuries incident to such voluntary services. Accordingly, any such services should be accompanied by a statement to the effect that the individual will not receive or be entitled to any compensation for these services. Such individuals may, however, enter into an independent contractor relationship with the Air Force and participate for compensation as authorized by applicable directives (45 Comptroller General 649).

8.3. Do not permit research involving prisoners of war or criminal inmates as human subjects in Air Force research protocols.

8.4. Do not use as subjects minors, mentally disabled persons, and others who cannot be fully informed and voluntarily give consent to participate unless the research measures used are intended to benefit the subject (10 U.S.C. 980(2)). Follow the procedures and guidance provided in AFI 40-403.

8.5. Note that in research conducted outside the United States involving foreign citizens as human subjects, the laws, customs, and practices of the country in which the research is conducted or the procedures required by this instruction, whichever are more stringent, take precedence. The research must meet the same standards of ethics and safety that apply to research involving US citizens conducted within the United States.

8.6. Submit any human-use protocols associated with nuclear weapon effects or chemical warfare agents to the Under Secretary of Defense for Acquisition, Director of Research and Engineering.

Section D—Consent Standards

9. Requirements. Adhere to the requirements established in 32 CFR 219.116.

9.1. Note that the informed-consent process is intended to give a subject all the information that he or she reasonably would want to know about a study; to ensure that the subject understands this information; and to give the subject an opportunity to agree or decline to participate in the study. The process is interactive, allowing the subject to ask questions and get answers from the investigator.

9.2. Remember consent must be voluntary. It must be the knowing consent of the individual who is sufficiently informed to be able to exercise free power of choice without undue inducement or any element of force, fraud, deceit, duress, or other form of constraint or coercion.

9.3. Obtain the subject's consent in writing.

9.4. Give the subject an adequate opportunity to read the consent document and ask questions. The subject, principal or associate investigator, and a witness not directly involved in the protocol must sign the consent document.

9.5. Note that the basis of voluntary, informed consent is complete and accurate disclosure of the nature of the protocol to the prospective human subject by a scientifically competent person in the presence of a witness not directly involved in the protocol. The consent documents testifies only to the fact that such a full and responsive discussion took place.

9.6. Retain, in the protocol records, sample copies of the consent documents, as approved by the HUC, as well as the actual consent documents signed by each subject. Provide a copy of the signed consent documents to the subject, the HUC, and file a copy in the subject's medical records along with enough documentation to clearly identify the protocol in which the subject participated.

9.7. Modify the sample consent format shown in AFI 40-403, attachment 3, as necessary, to make it conform to the principles outlined in this section. You must use this sample form, or a modified version of it.

9.8. As added protection for human subjects, include these safeguards:

- Assign a medical monitor (physician) to monitor all human subjects in protocols involving more than minimal risk. Before the protocol begins, the physician must conduct and record examinations and evaluations of human subjects as professional judgment dictates. The physician must be someone other than the principal or associate investigator. The physician has

full authority to terminate any subject's participation at any time death, injury, or bodily harm is likely to result.

- Provide apparatus, instruments, and personnel to deal with likely emergencies as required by the medical monitor.
- Provide medical treatment, including hospitalization if necessary, to any human subject who requires it as a result of his or her participation as soon as such need is recognized.

10. Records Maintenance. The performing organization must maintain all records documenting review, approval, conduct, and results of a research protocol involving human subjects. Such records represent an irreplaceable source of medical knowledge and are required for medico-legal deliberation.

Section E—Collaborative Research with Non-Air Force Organizations

11. Compliance:

11.1. The principal investigator must comply with this instruction, in collaborative studies with non-Air Force Federal agencies or civilian organizations that will involve Air Force subjects or Air Force facilities.

- Such studies must have an Air Force principal investigator (or coprincipal investigator).
- In addition, the local HUC and, if necessary, the Air Force HUC must review the study.

11.2. Air Force personnel may act as investigators in studies conducted outside Air Force facilities only if the commander approves participation as being in the best interest of the Air Force.

- If such studies involve human subjects, the responsible institutional review board must review and approve the studies according to Federal law and regulations.
- The organization commander must send a copy of the participation request and approval to HQ AFMOA/SGPT.

Section F—Contractor Studies

12. Procedures. This section sets out procedures for contractor research involving the use of human subjects. An organization may not award a contract for research involving the use of human subjects until the requirements of this instruction have been fully met.

12.1. Commanders who approve contractual research protocols involving human subjects must comply with the policies in AFPD 40-4 and the procedures in this instruction.

12.2. Contractors must safeguard the rights and welfare of all human subjects in research and other activities contracted with the Air Force by adhering to the requirements, policies, and procedures in 32 CFR 219 and this instruction.

- Each RDT&E organization must manage its contracts to ensure contractor compliance.
- The Air Force will not award any contract that involves the use of a human subject unless the contractor's HUC has reviewed and approved the proposed protocol, as directed by this instruction.
- The Air Force HUC must approve all contractor studies involving more than minimal risk.

12.3. The Air Force will not award a contract involving a human subject to an individual unless he or she is affiliated with or sponsored by an organization that can, and does, assume responsibility for that subject.

12.4. Any organization applying for a contract to conduct research involving a human subject must provide written assurances that it will abide by the policy for protection of human subjects as stated in this instruction.

- If the organization currently has an approved multiple-project assurance on file with the Department of Health and Human Service (DHHS), as described in 32 CFR 219.103(a), the organization must submit a statement to the Air Force contracting agency that such assurance will apply equally to the study under contract with the agency (**Attachment 3**). Attach to the protocol a copy of the multiple-project assurance from DHHS.
- If the organization does not currently have a multiple-project assurance on file with DHHS, the contractor must apply to HQ AFMOA/SGPT to obtain an assurance number before the award of the contract.

12.5. The contractor must ensure it has obtained all necessary clearances and permits and has properly coordinated with other agencies, whether Federal, state, or local.

12.6. Contractors must notify the US Air Force contracting agency of any misadventure or unanticipate medical event that coincides with or possibly results from using human subjects in a US Air Force-sponsored research protocol. Include all the information required in paragraph **7.7.**

- The contracting agency must notify HQ AFMOA/SGPT of all reported contractor misadventure or unanticipate medical events.

12.7. The contractor sends a copy of all contractor records documenting review, approval, conduct, consent forms, and results of any contract involving human subjects at risk to the sponsoring Air Force organization for storage at the end of the project.

ALEXANDER M. SLOAN, Lt General, USAF, MC
Surgeon General

Attachment 1

GLOSSARY OF REFERENCES, ABBREVIATIONS, ACRONYMS, AND TERMS

References

AFPD 40-4, *Clinical Investigation and Human Use in Medical Research*

AFI 40-403, *Clinical Investigations in Medical Research, Guidance and Procedures*

AFI 40-401, *The Use of Animals In DoD Programs*

32 CFR 219, *Federal Policy for the Protection of Human Subjects*

21 CFR 300-499, *Food and Drugs*

45 Comptroller General 649, *Personal Services-Private Contract v. Government Personnel-Research Subjects*

5 U.S.C. 5532, *Employment of Retired Members of the Uniformed Services; Reductions in Retired or Retainer Pay*

10 U.S.C. 980, *Limitation on Use of Humans as Experimental Subjects*

Abbreviations and Acronyms

AFI—Air Force Instruction

AFMC—Air Force Materiel Command

AFMOA—Air Force Medical Operations Agency

AFPD—Air Force Policy Directive

CFR—Code of Federal Regulations

DHHS—Department of Health and Human Services

DoD—Department of Defense

FDA—Food and Drug Administration

HUC—Human Use Committee

MAJCOM—Major Command

RDT&E—Research, Development, Test, and Evaluation

Terms

In addition to the terms defined in 32 CFR 219.102, the following terms apply to this instruction:—

Associate Investigator—An individual involved in a research study who collaborates with the principal investigator.

Consent—Informed consent given by a prospective human subject who has the legal capacity to give such consent. For active duty military personnel participating in a US Air Force protocol or collaborative study, there is no minimum age limitation.

Contract—Any contract, grant, interagency transfer, or other agreement by which funds chargeable to the Department of the Air Force are made available to any organization. Likewise, the term "contractor" includes any contractor, grantee, or other organization party to a contract.

Human Subject—As defined in 32 CFR 219, however, the term does not include:

- Military or civilian personnel who are qualified for and assigned to duties that specifically require testing, such as test pilots and test engineers.
- Persons performing assigned duties that involve inherent occupational hazards to health or exposure to potentially hazardous situations (for example, flight training, jump training, pressure-chamber training, and handling of explosives). If a research protocol contemplates use of such persons in an investigation not involving their assigned hazardous duties, the research protocol is evaluated under this instruction without consideration of the participant's hazardous-duty status.

Human Use Committee—A committee that evaluates the acceptability of studies involving human experimentation according to this instruction. The committee composition and function is consistent with that described for an Institutional Review Board in 32 CFR 219. The committee should not consist entirely of men or women, although the organization commander may waive this requirement when compliance is impractical. Except in cases of expedited review of protocols (32 CFR 219. 110) involving no more than minimal risk, at least a majority of the committee members must be present to conduct a meeting. If a committee member has a conflicting interest in a particular research protocol, he or she may not participate in the initial or continuing review of the research protocol except to provide information requested by the committee. When the committee reviews a protocol that includes more than minimal risk, a physician (other than the investigator) must be present as a member or ad hoc member of the committee.

Informed Consent Document—A written consent document, approved by the HUC, with which the investigator can obtain the legally effective consent of a subject or the subject's legally authorized representative. The informed consent document provides prospective subjects or their representatives with sufficient information to decide whether to participate in the proposed study.

Investigational Drugs and Devices—Drugs and devices used on human subjects that are not FDA-approved for marketing. Investigational drugs and devices may also include FDA-approved and well-accepted drugs or devices that are administered or used in tests on human subjects for nontherapeutic purposes (for example, tests that determine the potential effectiveness of drugs or devices in augmenting human tolerance to mission stress environment).

Medical Misadventure—An unauthorized deviation from an approved human use protocol that has the potential to cause or has brought about injury or loss of life to a study subject.

Medical Monitor—A physician observer, military or civilian, qualified by training and experience to provide care to research subjects under any conditions that may arise during research. He or she monitors human subjects during the conduct of the research. The medical monitor is also an advocate for the medical safety of the volunteers.

Non-US Citizens—Foreign nationals, excluding personnel on active duty.

Organization—Any federal, state, municipal, or other government agency, or any corporation, institution, foundation, agency, or other legally accountable entity.

Principal Investigator—A qualified individual who initiates a protocol and conducts a research study

based on the protocol after appropriate approval.

Unanticipated Medical Event—An unforeseeable, unpreventable event that causes injury or loss of life to a study subject, after all the guidelines set forth in an approved protocol have been followed. An adverse drug reaction is an example of such an event.

Attachment 2

SAMPLE PROTOCOL FORMAT

Title of Protocol

Date

1. Protocol, Task, or Work Unit, when applicable.
2. Principal Investigator.
3. Associate Investigator.
4. Medical Monitor.
5. Contractor and Facility, when applicable.
6. Protocol Objective. State purpose of the study.
7. Background and Relevance.
8. Impact Statement. Show how this protocol will contribute to the mission of the Air Force.
9. Experimental Plan. Provide at least the following information:
   a. List of equipment and facilities.
   b. Subjects (including number and selection criteria).
   c. Duration of the study.
   d. Experimental and data analysis procedures.
   e. Safety precautions or measures.
10. Medical Risk Analysis. Include the following items:
    a. Information for briefing subjects.
    b. Risk assessment (statement of the risk vs. benefits of the study).
11. References (bibliography).
12. Attachments. Attach the following items:
    a. Consent document.
    b. Curriculum vitae of principal investigator(s), associate investigator(s), and medical monitor(s).
    c. Contractor assurances, when applicable.
    d. Any other supportive documentation.

Attachment 3

CONTRACTOR ASSURANCES

A3.1. Assurances. The US Air Force requires assurances from contractor organizations conducting research involving human subjects that they will carry out initial and continuing review of all such research according to the policy and instruction contained in 32 CFR 219 and AFI 40-402. The contractor should send certification of the initial review and approval of the protocol by the contractor's Human Use Committee with the protocol when submitted. In any event, the contractor must submit the certification before the actual award of the contract or grant. An organization submitting a research protocol involving human test subjects must include one of the following applicable statements in the protocol:

A3.1.1. This protocol includes research involving human subjects as defined in AFI 40-402. Our organization has an accepted and currently valid multiple-project assurance on file with the Department of Health and Human Services (DHHS). The DHHS control number is _____. Our Human Use Committee has reviewed and approved this research protocol on _____, according to the assurance provided to DHHS, and will provide for continuing review as specified in the general assurance. A copy of the DHHS assurance is attached.

A3.1.2. This protocol includes research involving human subjects as defined in AFI 40-402. Our organization has an accepted and currently valid multiple-project assurance on file with DHHS. Our Human Use Committee has not yet reviewed this research protocol, but will do so on or about _____, according to the assurance provided to DHHS. It is understood that a certification of such review being completed will be required before the contract or grant can be awarded. A copy of the DHHS assurance is attached.

A3.1.3. This protocol includes research involving human subjects as defined in AFI 40-402. Our organization does not have an accepted and currently valid assurance on file with DHHS. We will be providing the required information to HQ AFMOA/SGPT to obtain a single-project assurance number for this protocol. It is understood that no research involving human subjects will be conducted until an assurance number has been issued by HQ AFMOA/SGPT.

A3.1.4. This protocol does not include research involving human subjects as defined in AFI 40-402, and we hereby certify that human subjects will not be used in any research performed under this grant or contract without proper assurances.